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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/922,960	08/03/2001	Michael W. Leviten	R-441	9830

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EXAMINER	
BERTOGLIO, VALARIE E	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 07/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	Application No.	Applicant(s)	
	09/922,960	LEVITEN, MICHAEL W.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-33,35-37,39 and 40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-33,35-37,39 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08/03/2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.

4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5)☐ Notice of Informal Patent Application (PTO-152)

6)☐ Other: _____.

DETAILED ACTION

This office action is in response to an after-final amendment filed 06/07/2004. **The amendment has been entered.** Claims 1-29,34 and 38 are cancelled. Claims 30-33,35-37,39 and 40 have been amended. Claims 30-33,35-37,39 and 40 are pending and under consideration. Upon further review of the instant claims and specification it is apparent that the application is not in condition for allowance. Therefore, prosecution is reopened. As new grounds of rejection are presented in this action that are not necessitated by applicant's amendment of the claims, this action is Non-Final.

Specification

The objection to the specification as set forth the previous office action mailed 01/02/2004 is maintained. Applicant has amended the specification to delete the phrase "(0 somites)" at page 52, loine 14. However, the text continues to conflict with Table 1. The text states that homozygous embryos resembled E7.5 embryos, which have 0 somites. Table 1 states that 3 homozygous mutants had 6-9 somites.

Claim Rejections - 35 USC § 101/112

Definitions:
[from REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS; repeated from http://www.uspto.gov/web/menu/utility.pdf]

"Specific Utility" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be *specific* in the absence of a disclosure of a specific DNA target. Similarly, a general statement of

diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

"Substantial utility" - a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material, which has a stated correlation to a predisposition to the onset of a particular disease condition, would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.

B. A method of treating an unspecified disease or condition. (Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. 101.)

C. A Method of assaying for or identifying a material that itself has no "specific and/or substantial utility".

D. A method of making a material that itself has no specific, substantial, and credible utility.

E. A claim to an intermediate product for use in making a final product that has no specific, substantial, and credible utility.

See also the MPEP § 2107 - 2107.02.

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30-33,35-37,39 and 40 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

The claims are directed to methods of making a transgenic mouse embryo whose genome comprises a homozygous disruption in the endogenous ubiquitin ligase E3 gene set forth in SEQ ID NO:1 (claim 39), the mouse embryo (claims 30-33,35,36 and 40), wherein the mouse embryo exhibits increased incidence of lethality during embryonic development. Claim 37 is drawn to a cell or tissue derived from the claimed mouse.

The instant specification has disclosed that the nucleotide sequence set forth in SEQ ID NO: 1 encodes a ubiquitin ligase E3 gene product. The instant specification has further contemplated that disruption of the nucleotide sequence set forth in SEQ ID NO: 1 in a mouse will produce a phenotype associated with the ubiquitin ligase E3 gene set forth by SEQ ID NO:1. The instant specification has purported that such mice may be used to identify agents that modulate or ameliorate a phenotype associated with a disruption in SEQ ID NO: 1. The specification has provided general teachings that the claimed transgenic mice may be used to identify agents that affect a phenotype related to the mice.

The instant specification has disclosed a transgenic mouse embryo whose genome comprises a disruption in SEQ ID NO: 1, wherein the mouse embryos fail to complete embryonic development. The instant specification has discussed that the mouse embryos of the instant invention provide methods for treating diseases associated with the disruption of an ubiquitin ligase E3 gene using a therapeutic agent that affects ubiquitin ligase E3 gene expression or function (page 5, lines 1-15). The specification also purports that the claimed

mouse embryos can be used a disease models to identify drugs (page 18, line 19-page 20, line 9). However, the evidence of record, while disclosing that the phenotypes exhibited by the claimed transgenic mice are consistent with symptoms associated with a ubiquitin ligase E3 gene, fails to provide a correlation between the embryonic lethal phenotype of the claimed mouse embryo, disruption of the ubiquitin ligase E3 gene set forth by SEQ ID NO:1 and any disease or disorder. The specification, therefore leaves the ordinary artisan to speculate and investigate the uses of the transgenic mouse encompassed by the claim. As set forth in the utility guidelines, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed. Similarly, a statement of therapeutic utility for an unspecified disease is non-specific.

The usefulness of the mutant mouse embryos as models is not clear without assessing that they specifically reflect a disease, requiring additional experimentation for the skilled artisan. The instant specification has failed to demonstrate that SEQ ID NO:1 encodes a protein with ubiquitin ligase E3 activity. In fact, Merla has taught that the nucleic acid sequence set forth in SEQ ID NO:1 encodes an RCC1-like G exchanging factor (Human Genetics, 2002, Vol. 110, page 430, col. 2 last paragraph; refer also to Genbank Accession No. AF4410456). The sequence taught by Merla in Genbank Accession No. AF4410456 is 100% identical to SEQ ID NO:1. It is not clear, therefore, that SEQ ID NO:1 encodes a ubiquitin E3 ligase, rendering the claims as lacking a credible utility. Furthermore, the specification and art of record has failed to correlate SEQ ID NO:1 with any disease. As set forth in the utility guidelines, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed. Similarly, a statement of therapeutic

utility for an unspecified disease is non-specific. The phenotype of embryonic lethality associated with the claimed mice does not appear to be specific to any disease. Therefore, no correlation has been made between the purported ubiquitin ligase E3 gene and any specific disease and therefore, the claimed mice lack a specific utility.

Furthermore, it would require further research for the skilled artisan to determine whether the protein encoded by SEQ ID NO:1 is a ubiquitin ligase and what its in vivo role is. The phenotype claimed is increased incidence of embryonic lethality. The specification fails to disclose how results from an assay indicating a compound prevents the claimed increased embryonic lethality would be useful. What would one do with a compound that prevents the embryonic lethality associated with the claimed transgenic mouse embryo? The specification has not described the mouse embryos as having any particular use and not described any particular disease model. It would require further research to determine if the phenotype of embryonic lethality can even be rescued. As such, under the utility guidelines set forth above, requirement for further research or experimentation renders the claimed invention as lacking a substantial utility. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities

The evidence of record has not provided any other utilities for the transgenic mouse encompassed by the claims that are specific and substantial.

In light of the above, the skilled artisan would not find the asserted utility of the transgenic mouse, cells and tissues encompassed by the claims to be credible, specific or substantial.

Claims 30-33, 35-37, 39 and 40 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial utility or a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 39 and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 39 is unclear because the preamble encompasses a method of producing a transgenic mouse embryo comprising an extrachromosomal gene disruption. However, the method steps are directed to making a transgenic mouse embryo whose genome comprises a gene disruption.

Claim 39 is unclear because a pseudopregnant mouse cannot give birth (see step (c)). Only a pregnant mouse can give birth. Claim 40 depends from claim 39.

Claim 39 is rejected as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Step (d) requires mating chimeric mice comprising a heterozygous disruption in the ubiquitin ligase E3 gene. It is standard in the art, and supported by the specification (page 52), that the chimeric heterozygotes are mated to wild-type mice. Therefore, the breeding in step (d) results in a heterozygous non-chimeric mouse rather than a mouse comprising a homozygous disruption. An additional step of mating two heterozygotes is needed to obtain a homozygote.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Valarie Bertoglio
Examiner
Art Unit 1632

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